

Wake-Up Test Decrease Shunts Insertion During Carotid Endarterectomy Under General Anesthesia

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Luigi Vetrugno, MD,¹ Elena Di Luca, MD,¹ Daniela Drigo, MD,²
Valtiero Fregonese, MD,³ Nevio Gonano, MD,³ and Francesco Giordano, MD¹

Abstract

Objective: The use of locoregional anesthesia versus general anesthesia (GE) in carotid endarterectomy (CEA) has been a debatable issue in clinical studies for the past several years. In our study, GE with wake-up tests (WUTs) during carotid cross-clamping was used instead of stump pressure (SP) to directly assess the neurological status of the patient to determine whether shunting was needed. Our study assessed the percentage of patients under light sedation and mechanically ventilated needing shunting based on WUT compared to a systolic stump pressure (SPs) cutoff value of ≤ 40 mm Hg. Design: Retrospective, observational study. **Setting:** University hospital clinic. **Participants:** Three hundred fifty-one patients (American Society of Anesthesiologists physical class II-III) with carotid artery stenosis scheduled for CEA under GE. **Interventions:** The WUT was used to assess the neurological status in patients undergoing CEA, which involved the gradual reduction of depth of anesthesia until the patient was capable of responding to a verbal stimulus and provide full collaboration while only receiving remifentanyl. A positive WUT indicated that patient was not able to carry out the order. **Measurements and Main Results:** Of 343 patients, 20 (5.8%) were shunted due to a positive WUT after cross-clamping in comparison to 45 patients (12.8%) based on the SPs ≤ 40 mm Hg criteria. **Conclusion:** Wake-up test can be used to directly assess the neurological status in patients undergoing CEA to determine whether shunting is required. Our results showed that less patients required shunting based on WUT compared to the SP criteria.

Keywords

wake-up test, stump pressure, carotid endarterectomy, general anesthesia, stroke

Introduction

In the midst of conflicting study results in literature,¹⁻⁴ the GALA trial^{5,6} recently showed that the differences in neurological outcomes between local/regional anesthesia (LA) versus general anesthesia (GA) for carotid endarterectomy (CEA) were not significant. We have been performing CEA under GA with a "wake-up test" (WUT) in our department for the past 10 years.⁷ Previous studies have shown that the WUT can successfully be used during carotid cross-clamping in assessing the patient's neurological status to determine whether shunting is required during surgery.⁸⁻¹⁰ This method of awakening patients during surgery has widely been used in scoliosis surgery to ensure that normal spinal cord function is maintained.¹¹ Previous studies have reported other criteria during surgery under GA to determine the need for shunting, which include carotid artery stump pressure (SP),¹²⁻¹⁵ electroencephalography (EEG),^{16,17} transcranial Doppler sonography (TCD),^{18,19} somatosensory-evoked potential (SSEP), and near-infrared spectroscopy (NIRS).²⁰⁻²³ These methods, however, assess the neurological status of the patient indirectly and at a higher cost (with exception to SP). No single method has shown to offer

better surgical outcomes to date.²⁰⁻²² The systolic SP (SPs) criteria is generally used for selective shunting insertion under GA^{15,16} when SP < 50 mm Hg. This cutoff value, however, includes false-positive and false-negative rates. Shunting may prevent cerebral hypoperfusion due to cross-clamping; however, the shunt procedure increases the risk of stroke due to induced vascular damage and emboli passing through the shunt from the common carotid artery.¹⁸ In our study, GE with WUT during carotid cross clamping was used instead of SP to directly assess the neurological status of the patient to determine the need for shunting. The aim of the study was to assess

¹ Cardiothoracic and Vascular Anesthesia, University-Hospital of Udine, Udine, Italy

² Institute of Hygiene and Epidemiology, DPMSC, University-Hospital of Udine, Udine, Italy

³ Department of Vascular Surgery, University-Hospital of Udine, Udine, Italy

Corresponding Author:

Luigi Vetrugno, Cardiothoracic and Vascular Anesthesia, University-Hospital of Udine, Udine, Italy

Email: vetrugnoluigi@katamail.com

the percentage of patients under light sedation and mechanically ventilated needing shunting based on WUT compared to the SPs ≤ 40 mm Hg criteria.²⁴

Patient Population and Methods

Carotid endarterectomy under GA with a WUT has been used in our department of anesthesia and vascular surgery since 1998 on over 1200 patients (American Society of Anesthesiologists physical class II-III). Our retrospective observational study was based on 351 patients undergoing planned CEA from January 2005 to December 2008. All patients gave informed signed consent. Patients undergoing emergency surgery or combined CEA and coronary artery bypass graft (CABG) surgery were excluded from the analyses. The WUT was used to assess the neurological status in patients undergoing CEA, which involved the gradual reduction of depth of anesthesia until the patient was capable of responding to a verbal stimulus and provide full collaboration (ie, open eyes, nod of head to answer simple questions, tighten hand around the doctors finger, and so on) while only receiving remifentanyl. A positive or abnormal WUT indicated that patient was not able to carry out the order, thus a shunt was indicated. This test is similar to the one used during spinal surgery to detect neurological damage.¹¹ Systolic stump pressure measurements were also recorded for each patient. The patient's neurological function was closely monitored every minute for the first 3 minutes, then at 3-minute intervals after carotid clamping. A temporary carotid shunt was placed by the surgeon when a neurological deficit was detected and not reversed by an arterial blood pressure increase. Carotid shunts were only placed in patients with a positive WUT (even if SPs >40 mm Hg). Shunts were not placed in patients showing a negative WUT (even if SPs ≤ 40 mm Hg). Standard anesthesia monitoring consisted of 2-lead electrocardiography (II/V5), pulse oximetry, invasive systemic arterial pressure (AP) monitoring, and multigas analysis. A radial artery catheter was placed in all patients prior to induction of anesthesia to obtain invasive AP. Under Bispectral Index monitoring (BIS—Aspect Medical Systems, Inc, Newton, Massachusetts), anesthesia was then induced with propofol target-controlled infusion system (TCI; Alaris Asena PK; Alaris Medical Systems, San Diego, California). The initial central nervous system effect-site target concentration was set at 3 to 4 $\mu\text{g/mL}$ to obtain a BIS value of 40 to 60. After 2 minutes of propofol infusion, remifentanyl was administered at an initial effect site concentration of 5 to 7 ng/mL based on a 3-compartment pharmacokinetic algorithm described by Minto.²⁵⁻²⁷ Pharyngeal-laryngeal topical anesthesia was used, followed by tracheal intubation. Propofol TCI was lightly reduced after induction, and anesthesia was maintained only with remifentanyl infusion. The surgeon then applied superficial local anesthesia on the ipsilateral side of the neck. A clamp was first applied to the external carotid artery, then to the common carotid artery after systemic 10 000 IU of heparin. A 19-gauge needle was inserted in the common carotid artery to obtain SP measurements. The common carotid artery SP was

compared to the radial artery systolic pressure (APS). An accurate SP was based on a flat waveform, indicating the absence of collaterals filling the carotid artery between the clamps. Bispectral Index monitoring was used to pilot the WUT. Neurological assessment during the WUT was maintained only with remifentanyl; propofol was added at a rate of 1.0 to 1.2 $\mu\text{g/mL}$ in patients showing discomfort. Endarterectomy was repaired with a patch graft in all patients. Patients were regularly monitored and assessed by the vascular surgeon in the postoperative vascular ward.

Data Analysis

Statistical analysis was performed by using the Statistical Analysis System (SAS; SAS Institute Inc, Cary, North Carolina) statistical package. Validity measures were determined for SPs; WUT was used as gold standard. Sensitivity was calculated as the proportion of patient with SPs ≤ 40 mm Hg and a positive WUT among all those with a positive WUT. Specificity was based on the proportion of patients with SPs >40 mm Hg and a negative WUT among all those with a negative WUT. Ninety-five percent confidence intervals (95% CI) for validity measures were calculated using the exact probabilities of the binomial distribution. Receiver operating characteristic (ROC) curves were determined for SPs >40 and SPs ≤ 40 based on sensitivity and 1-specificity. A new variable "SPs level" was created: SPs level was 0 if SPs ≤ 40 mm Hg and 1 if SPs >40 mm Hg. Fisher test was used to assess the associations between SPs level and adverse events within a 24-hour post-op period. The significance level of the test was $P \leq .05$. Multiple logistic regression was used to estimate the risk of no adverse effect in the following 2 situations: when the SPs and WUT criteria suggested placing the shunt that was actually positioned and when only the SPs criteria suggested placing the shunt that was not placed.

Results

Statistical Date

Patient demographics and comorbidities data are listed in Table 1. A total of 351 patients underwent CEA under GA using the WUT (Table 2): 20 (5.8%) patients showed a positive WUT, which was indicative of neurological deterioration and hence were shunted; 323 (92%) patients were not shunted because of a negative WUT; 8 (2.3%) patients had a dubious WUT, so the surgeon decided to complete the surgery without a shunt. In 6 of these patients SPs was >40 mm Hg, in the other 2 patients SPs was <40 mm Hg; in these last 2 cases, the surgical team should have placed the shunt. Twenty percent of patients (4 of 20) with SPs >40 mm Hg (false negative) required shunting because of a neurological change (positive WUT) versus 8.4% (27 of 323) with SPs ≤ 40 mm Hg (false positive) with a negative WUT. Based on the SPs ≤ 40 mm Hg criteria, 12.8% (45 of 351) of patients would have undergone a shunt during surgery compared to 5.8% (20 of

Table 1. Patients characteristics

Patient demographic and clinical data	
Variable	(%)
Patients numbers	351 (100)
Men	235 (67)
Woman	116 (33)
Artery to be operated (right side)	174 (49.7)
	Mean $\pm$ SD
Age (years)	72 $\pm$ 8
Stump pressure systolic (mm Hg)	52 $\pm$ 18
Duration of carotid clamping (minutes)	42 $\pm$ 10
Duration of surgery (minutes)	109 $\pm$ 16
Patient comorbidities	
Disease	Frequency (%)
Hypertension	295 (84)
Diabetes	80 (23)
Myocardial infarction	27 (7.7)
Unstable angina pectoris	26 (7.4)
Indications for CEA	
Stroke	55 (15.6)
Transient ischemic attack	65 (18.5)

NOTE: CEA = carotid endarterectomy.

Table 2. Results of the Wake-Up Test and Stump Pressure Criteria to Determine the Necessity of Shunting During Carotid Endarterectomy

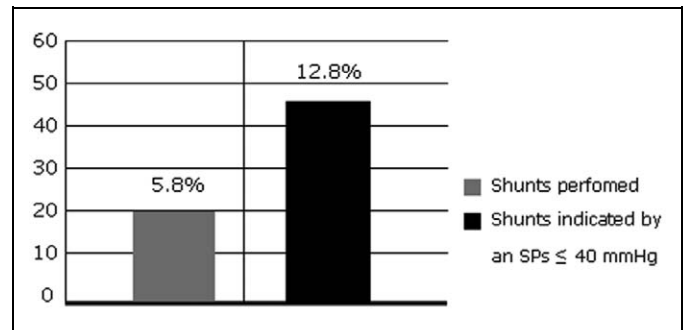
Stump Pressure (SPs) mm Hg	Wake-Up Test Negative (%)	Wake-Up Test Positive (%)	Wake-Up Test Dubious (%)	Total
SPs > 40	296 (91.6)	4 (20)	6 (75)	306
SPs $\leq$ 40	27 (8.4)	16 (80)	2 (25)	45
Total	323	20	8	351

NOTE: SPs = systolic stump pressure.

343) of patients that were actually shunted (Figure 1), a difference that was statistically significant ($P < .05$). Shunts were not positioned in 27 (8.4%) patients with an abnormal SPs and a negative WUT. The SPs sensitivity was 80%, negative predictive value was 98.7%, and specificity was 90.4% (IC_{95%} 87.2%-93.6%). The SPs positive predictive value was 36.7% (IC_{95%} 23.2%-50.2%), while the negative predicting value was 98.7% (IC_{95%} 96.2%-99%). Fisher test did not show a statistically significant difference between frequency of adverse events in patients with an "SPs level" equal to 0 or 1 ($P > .05$). With regard to the anesthetic drug effects, remifentanyl TCI at 2 to 2.5 ng/mL (equal to 0.1-0.15 μ g/kg per minute total intravenous anesthesia, [TIVA]) was found to provide satisfactory tracheal tube tolerance during the test, alleviating pain and discomfort associated with intubation. Propofol was either switched off or maintained at a rate of 1 to 1.2 μ g/mL.

Postoperative Complication

The postoperative complications are listed in Table 3. Stroke or transient ischemic attack (TIA) was seen in 3 patients (0.8%);

**Figure 1.** Of 343 patients, 20 (5.8%) were shunted based on a positive wake-up test (WUT) after cross-clamping in comparison to 45 patients (12.8%) based on stump pressure (SP) $\leq$ 40 mm Hg.

one of which (61-year-old woman) died on the third day post-op after developing epilepsy due to cerebral hemorrhage. Cardiovascular problems (ie, myocardial ischemia, atrial fibrillation, hypohypertension, or hemodynamic instability) occurred in 8 patients (2.3%). Eighteen patients (5.1%) showed local adverse event due to the surgery of the neck region (ie, neck hematoma or nerve paresis), including 2 cases of facial nerve palsy (mandibular branch; 0.6%), 2 cases of hypoglossal nerve deficit (0.6%), 3 cases of recurrent laryngeal nerve paralysis (0.8%), 4 cases (1.1%) of temporary vocal cord palsy, and 3 cases of pharynx palsy. The incidence of hematoma necessitating reexploration was 1.1%. None of the patients showed patch or wound infections.

Discussion

Wake-up test during carotid cross-clamping under GA was used as the determining criteria for shunting instead of SPs. Wake-up test was found to be a safe and effective method to directly assess the neurological status of the patient undergoing CEA surgery under GE. The need for shunting based on the WUT criteria was statistically less than that based on the traditional SP criteria (5.8% vs 12.8%), thus limiting the potential risks involved with shunt insertion. Studies have shown several criteria to determine the need for carotid shunt placement during surgery, which include SP, EEG, TCD, SSEP, and NIRS.¹²⁻²³ In our cohort, shunts would have been placed in 12.8% of patients using the SPs $\leq$ 40 mm Hg criteria; however, less than half of these (5.8%) actually underwent shunting based on the WUT criteria. Moreover, 20% of patients (4/20) with a normal SPs > 40 mm Hg criteria (false negative) required shunting due to neurological change (positive WUT). In addition, 8.4% (27 of 323) of patients showed an abnormal SPs $\leq$ 40 mm Hg criteria (false positive) with a normal negative WUT, which did not require a shunt. In comparison, Evans et al²⁸ reported a very low false-negative rate of 3.2% for SPs > 50 mm Hg. The main difference with other studies was the fact that our patient was intubated. Our vascular surgeons tend to prefer the direct approach of assessing neurologic change in awake patients during CEA because it is highly indicative of cerebral perfusion. The idea is the need to arrange an anesthesia

Table 3. Postoperative Complications, %

Death			1 (0.28)
Neurological dysfunctions	Major	Stroke	2 (0.56)
		TIA	1 (0.28)
	Minor	Cranial nerves palsy	10 (2.8)
		Mandibular branch of the facial nerve	2 (0.56)
Cardiovascular dysfunctions	Major	Hypoglossal nerve	2 (0.56)
		Myocardial infarct	2 (0.56)
	Minor	Hypotension/hypertension	5 (1.4)
		Atrial fibrillation	1 (0.28)
Surgery dysfunctions	Major	Neck hematoma reexploration	2 (0.56)
	Minor	Minor neck hematoma	2 (0.56)
Infection	Patch/wound		0
	Systemic		0

NOTE: TIA = transient ischemic attack.

plan incorporating the major advantage of local anesthesia (neurological monitoring) and the main benefits of GA (optimal tolerance for patients and definitive and safe control of airways). The unique pharmacokinetic profile of remifentanyl in terms of analgesic plane without change in term of recovery time make it possible. Our study cannot be used to confirm that SPs <40 mm Hg criteria reported in previous studies¹⁵⁻²⁴ should be taken as a cutoff threshold for carotid shunting under GA. We are not certain that SPs ≤40 mm Hg for shunt placement in our patients under remifentanyl and mechanically ventilated are applicable to patients under deep GA.

Conclusion

In summary, WUT can be used to directly assess the neurological status in patients undergoing CEA to determine whether shunting is required. Our results showed that significantly less patients required shunting based on WUT compared to the SP criteria. Future studies are needed to confirm the advantages of using WUT to assess intraoperative cerebral blood flow.

Limitation of Study

Minor neurological changes during clamping could have occurred in our cohort and not adequately assessed with the WUT. Moreover, the WUT assessed neurological impairment using consciousness and hemiparesis in patients that were intubated, thus aphasia could not be assessed. The postoperative complications in our study, that is, neurologic, cardiovascular, and so on (Table 3) was minimal, which may be due to the limited number of patients in our analysis and that the neurological outcomes were subject to bias.

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Declaration of Conflict of Interests

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